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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,601	05/01/2001	Alfred S. Lewin	36689.140	7183

27683 7590 09/27/2006

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,601	LEWIN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *2,3,5 and 9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,8,14-42,58 and 59* is/are rejected.

7)☒ Claim(s) *4 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/20/01, 12/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *see attached squence alignment*.

DETAILED ACTION

Election/Restrictions

In the requirement for restriction/election filed 09/09/2005, Group I was subject to a further restriction wherein Applicants were required to elect a single ribozyme target sequence from claims 2, 3, 5, 7-13 and were required to elect a single ribozyme sequence from claims 3 and 4. Claim 3 was mistakenly included as a ribozyme target sequence but was properly included as a ribozyme sequence along with group 4.

Applicant's election with traverse of group I, claims 1-42, and election of a single ribozyme target SEQ ID NO:88 and a single ribozyme sequence SEQ ID NO:100 in the reply filed on 05/23/2006 is acknowledged.

The traversal is on the ground(s) that a further election of a Markush group for incorrect Markush language is improper. The additionally restriction requirement was not imposed because of improper Markush language but because claims 2-5 and 7-13 were not considered to be a proper genus/Markush. As stated in the prior requirement for restriction/election, MPEP 803.02 states that if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 300 (CCPA 1980); and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to

examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structure feature disclosed as being essential to that utility.

Here, because claims 2, 5 and 7-13 specifically claims ribozymes target mRNA as listed and the ribozyme targets are considered to be unrelated since ribozyme target is each is structurally and functionally independent do not share a common structure, the Markush/genus of the mRNA in 2, 5 and 7-13 are not considered to constitute a proper genus, and are therefore subject to restriction. Furthermore, a search of more than one (1) of the ribozyme target sequences claimed presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination.

The traversal is additionally on the ground that a search of more than one nucleotide sequence is not an undue burden on the Office. Applicant recites MPEP 2434 as support for the Examiner to perform a search of more than one sequence claimed. This is not found persuasive because the complex nature of the search and corresponding examination of more than one (1) of the claimed ribozyme sequences and more than one of the claimed mRNA target sequences. Applicant is correct in that MPEP 2434 states "..the Commissioner has partially waived the requirements of 37 CFR 1.141 and will permit a reasonable number of such nucleotide sequences to be

claimed in a single application. Under this policy, in most cases, up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction." However, MPEP 2434 further states that a reasonable number of sequences selected can be less than 10 "...due to the complex nature of the claimed material."

In the instant case, a search of more than one ribozyme sequence and a search of one ribozyme target sequence are considered to be a reasonable number of sequences for examination. Contrary to Applicants' assertion that "[t]he searching process allows one to submit any number of sequences for electronic search and that search is able to scan millions of documents and sequence in a matter of minutes to identify references that each homologous, related, or identical sequences", a search to identify prior art sequences of more than one ribozyme sequence and more than one ribozyme target sequence *and* the corresponding examination of the results would place an undue burden on the Office and the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Application

Claims 1-59 are pending. Claims 1, 4, 8, 14-42, and new claims 58-59 are currently under examination. Claims 2-3, 5, 9-13 are withdrawn as being drawn to a non-elected invention.

Claim Objections

Claims 4 and 5 are objected to as reciting non-elected subject matter. Claims 4 and 5 should be rewritten deleting any non-elected subject matter.

Claim 4 is objected to as being dependent upon a withdrawn base claim and reciting non-elected subject matter, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 14-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-3, 9-15, 17-20 and 22-38 of U.S. Patent No. 6,225,291. Although the conflicting claims are not

identical, they are not patentably distinct from each other because the instant claims and the claims of the patent are drawn to patently indistinguishable subject matter.

Claim 1 is drawn to a ribozyme that specifically cleaves an mRNA encoding a polypeptide that cause or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye, wherein the ribozyme is a hammerhead or hairpin ribozyme (claims 14-15) and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter, wherein the vector is a viral vector, wherein said viral vector is an adeno-associated viral vector (claims 16-18), wherein said promoter element directs expression of said polynucleotide in a retinal, photoreceptor cell, a rod or cone cell, a Mueller or retinal epithelium cell (claims 19-22), wherein said promoter element comprises a mammalian rod opsin promoter element, a constitutive or inducible promoter (claim 23-24), wherein a virus comprises said ribozyme or polynucleotide comprising said ribozyme, wherein said virus is adenovirus or an adeno-associated virus (claims 24-29). The instant claims are further drawn to a host cell, wherein said host cell is mammalian, a human cell, a retinal cell, wherein said retinal cell is a photoreceptor cell (claims 30-35) and drawn to composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-39) and a kit wherein said kit comprises a composition and further comprises a device for delivering said composition to the eye (claims 40-42).

Claims 1-3 of U. S. Patent No. 6,225,291 are drawn to a ribozyme that specifically cleaves an mRNA encoding a mutant rod opsin polypeptide in a retinal cell of a mammalian eye and drawn to a catalytic RNA molecule that specifically cleaves an

mRNA encoding a mutant rod opsin polypeptide in a retinal cell of a mammalian eye wherein the catalytic RNA is a hammerhead or hairpin ribozyme (claims 9-11). The claims of Patent '291are further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter, wherein the vector is a viral vector, wherein said viral vector is an adeno-associated viral vector (claims 12-15), wherein said promoter element directs expression of said polynucleotide in a retinal, photoreceptor cell, a rod or cone cell, a Mueller or retinal epithelium cell (claims 16-19), wherein an adeno-associated virus comprises said ribozyme or polynucleotide comprising said ribozyme, wherein said adeno-associated viral vector comprises a polynucleotide operably linked to at least a first regulatory element (claims 20 and 22-23). The claims of Patent '291 are further drawn to a host cell, wherein said host cell is mammalian, a human cell, a retinal cell, wherein said retinal cell is a photoreceptor cell (claims 24-29) and drawn to composition, wherein said composition further comprises a pharmaceutical excipient (claims 30-33) and a kit wherein said kit comprises a composition comprises said ribozyme (claims 34-38).

The claims of the instant application are broadly drawn to a ribozyme that cleaves a broad genus of mRNA encoding a polynucleotide that causes or contributes to the disease, disorder or dysfunction of a cell or tissue of a mammalian eye. Claims 1-3, 9-15, 17-20 and 22-38 of Patent '291 are drawn to a ribozyme that cleaves a species of mRNA encoding a polypeptide that causes or contributes to the disease, disorder or dysfunction of a cell or tissue of an eye, namely a mRNA encoding a mutant rod opsin polypeptide in a retinal cell of the eye. MPEP 2132.02 states in part: "A

generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." The species in that case will anticipate the genus. In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989).

Therefore, one of ordinary skill in the art would have found it obvious to make compounds of the instant application and would have been motivated and would have expected success because Patent '291 disclose specific and successful embodiments of the claimed invention.

Thus, claims 1 and 14-42 of the instant application are anticipated by claims 1-3, 9-15, 17-20 and 22-38 of Patent '291.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 14-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, MPEP §2163 states, in part "...a patent specification must describe the claimed invention in sufficient detail that one

skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." Moreover, the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by "...disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between functional and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus."

The claims are drawn to a broad genus of ribozymes that specifically cleaves mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye.

The instant claims and specification fail to provide adequate written description of the infinite number of ribozyme molecules commensurate in scope with the breadth of the instant invention: cleavage of any mRNA encoding an infinite number of polypeptides that causes or contributes to the disease, disorder or dysfunction of a cell or a tissue in a mammalian eye from any specie.

The specification as filed discloses in Tables 4-6, examples of specific ribozyme target sequences and discloses sequences of ribozyme molecules. The specification further discloses in example 7, a specific embodiment of a ribozyme targeted to IGF-I receptor wherein said ribozyme is delivered to murine retinal cells and a decrease in neovascularization on the surface of the retina.

The specification does not provide a core structure sequence of a ribozyme that is capable of cleaving any mRNA encoding any polypeptide that causes or contributes to the disease, disorder or dysfunction of a cell or a tissue of a mammalian eye. Therefore in only disclosing minimal examples of ribozyme sequences and one specific embodiment of a decrease in neovascularization of a murine retina after treatment with ribozyme target to a gene encoding IGF-I, the specification does not provide adequate written description for the infinite number of ribozyme sequences in the genus that provide the asserted activity of cleavage of any mRNA encoding any mRNA encoding any polypeptide that causes or contributes to the disease, disorder or dysfunction of a cell or a tissue of a mammalian eye.

Moreover, MPEP §2163 states, in part: "[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004).

Therefore, in the instant application, Applicants have not shown possession of the entire claimed genus of ribozyme sequences that targets any mRNA encoding any polypeptide that causes eye disease in any mammal.

Applicants are reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 14, 30-34 and 36-39 are rejected under 35 U.S.C. 102(a) as being anticipated by Caballero et al. (Investigative Ophthalmology and Visual Science 1991).

The instant claims are drawn to a ribozyme that specifically cleaves an mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye (claim 1), wherein the ribozyme is a hammerhead ribozyme (claim 14). The instant claims are further drawn to a host cell, wherein said host cell is mammalian, a human cell or a retinal cell (claims 30-34) and

drawn to composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-39).

Caballero et al. teach a ribozyme that decreases expression of IGF-I in human retinal vascular endothelial cells (see conclusion 4481-B91). Caballero et al. teach the ribozyme is a hammerhead ribozyme and further teach a composition comprising said ribozyme and a liposome for deliver to a human host cell (see methods 4481-B91).

Thus, Caballero et al. anticipates claims 1, 14, 30-34 and 36-39 of the instant application.

Claims 1, 14-18, 24-33 and 36-39 rejected under 35 U.S.C. 102(e) as being anticipated by Pavco et al. (U.S. Patent No. 6,346,398).

The instant claims are drawn to a ribozyme that specifically cleaves an mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye (claim 1), wherein the ribozyme is a hammerhead or hairpin ribozyme (claims 14-15) and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter, wherein the vector is a viral vector, wherein said viral vector is an adeno-associated viral vector (claims 16-18), wherein said is a constitutive or inducible promoter (claim 24), wherein a virus comprises said ribozyme or polynucleotide comprising said ribozyme, wherein said virus is adenovirus or an adeno-associated virus (claims 24-29). The instant claims are further drawn to a host cell, wherein said host cell is mammalian or a human cell (claims

30-33) and drawn to a composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-39).

Pavco et al. teach a ribozyme targeted to and specifically cleaves a gene encoding a VEGF mRNA (see Table II and Examples 7-8). Pavco et al. teach VEGF is responsible for retinopathy (see col. 14, lines 53-60). Pavco et al. teach the ribozyme is preferably a hairpin or hammerhead ribozyme (see col. 5, lines 5-10) and teach a viral vector, specifically an adeno-viral vector, comprising said ribozyme (see col. 6 and 13, lines 33-52 and 36-60, respectively) and teach the use of viral particles comprising said ribozyme to deliver said ribozyme to target cells (see col. 14, lines 1-15). Pavco et al. additionally teach human host cells comprising said ribozymes and teach compositions comprising lipofectamine and said ribozymes (see Example 2).

Thus, Pavco et al. anticipates claims 1, 14-18, 24-32 and 36-42 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 8, 14-16, 30-32, 36-37 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wraight et al. (WO 00/78341) and Thompson et al. (U.S. Patent No. 5,750,390).

The instant claims are drawn to a ribozyme that specifically cleaves an mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye (claim 1), wherein the ribozyme specifically cleaves an mRNA that comprises a nucleotide sequence having SEQ ID No. 88, wherein the ribozyme is a hammerhead or hairpin ribozyme (claims 14-15) and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter (claim 16). The instant claims are further drawn to a host cell, wherein said host cell is mammalian or a human cell (claims 30-32) and drawn to a composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-37 and 39) and drawn to a kit wherein said kit comprises a composition (claims 40-41).

Wraight et al. teach an antisense oligonucleotide that binds to and inhibits expression of a sequence comprising SEQ ID NO. 88 (see attached sequence alignment, IGF-I oligonucleotide #2501) and teach IGF-1 is involved in neovascularization of the retina (see page 21, lines 6-15). Wraight et al. does not teach the oligonucleotide is a ribozyme and further does not teach a vector comprising a promoter and a ribozyme, a host cell comprising a ribozyme, a composition or a kit comprising a ribozyme.

Thompson et al. teach ribozyme molecules and teach the enzymatic nature of ribozymes is advantageous over technologies such as antisense technologies (see col.

2). Thompson et al. further teach ribozymes can be hammerheads or hairpins (see col. 13), teach expression vectors comprising promoters and ribozymes (see col. 8), and teach pharmaceutical compositions comprising liposomes and ribozymes (see col. 10).

It would have been obvious to one of skill in the art to substitute a ribozyme for an antisense molecule, as taught by Thompson et al., to inhibit expression of a gene encoding IGF-I, a polypeptide involved in neovascularization of the retina, as taught by Wraight et al.

One of skill in the art would have been motivated to use a ribozyme molecule to target IGF-I instead of a antisense, because Thompson et al. teach ribozymes are advantageous over antisense oligonucleotides since the effective concentration of ribozymes necessary to effect therapeutic treatment is lower than that of antisense oligonucleotides (see col. 2). Further, one of skill in the art would have been motivated to use a ribozyme because the ribozyme is a highly specific inhibitor and has the ability to act enzymatically: a single ribozyme molecule is able to cleave many molecules of a target RNA.

Finally, one would have had a reasonable expectation of success at making a ribozyme targeted to IGF-I given that the IGF-I sequence was known, as evidenced by Wraight et al. making specific inhibitory sequences targeted to IGF-I, and further given that Thompson et al. provides a detailed disclosure of how to make any ribozyme targeted to any sequence.

Thus, in absence of evidence to the contrary, the invention would have been *prima facie* evident to one of ordinary skill in the art.

Claims 1 and 14-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pavco et al. (U.S. Patent No. 6,346,398) and Kido et al. (Current Eye Research 1996).

The instant claims are drawn to a ribozyme that specifically cleaves an mRNA encoding a polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye (claim 1), wherein the ribozyme is a hammerhead or hairpin ribozyme (claims 14-15) and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter, wherein the vector is a viral vector, wherein said viral vector is an adeno-associated viral vector (claims 16-18), and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter, wherein the vector is a viral vector, wherein said viral vector is an adeno-associated viral vector (claims 16-18), wherein said promoter element directs expression of said polynucleotide in a retinal, photoreceptor cell, a rod or cone cell, a Mueller or retinal epithelium cell (claims 19-22), wherein said promoter element comprises a mammalian rod opsin promoter element, a constitutive or inducible promoter (claim 23-24), wherein said promoter is a constitutive or inducible promoter, wherein a virus comprises said ribozyme or polynucleotide comprising said ribozyme, wherein said virus is adenovirus or an adeno-associated virus (claims 24-29). The instant claims are further drawn to a host cell, wherein said host cell is mammalian, a human cell or a retinal cell (claims 30-35) and drawn to a composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-39) and drawn to a

kit wherein said kit comprises a composition and further comprises a device for delivering said composition to the eye (claims 40-42).

Pavco et al. is relied upon for the reasons stated above in the 102(e) rejection. Further, Pavco et al. teach Pavco et al. teach use of ribozyme as diagnostic reagents and further teach a delivery device, such as filter disks surgically implanted into a mammalian eye for delivery of said ribozyme composition (see col. 21 and Example 11). Pavco et al. does not teach a vector wherein said promoter element directs expression of said polynucleotide in a retinal cell, a photoreceptor cell, a rod or cone cell, a Mueller cell or wherein said promoter comprises a mammalian rod opsin promoter element.

Kido et al. teach use of a viral vector comprising a mouse opsin promoter (see Figure 1). Kido et al. teach said opsin promoter directs expression in photoreceptor cells, which comprise rod and cone cells, and directs expression in Mueller cells (see page 838 second column and Figure 8C).

It would have been obvious to one of ordinary skill in the art to incorporate the mammalian opsin promoter, as taught by Kido et al. into a viral vector expressing a ribozyme targeted to cells of a mammalian eye, as taught by Pavco et al.

One of skill in the art would have clearly been motivated to incorporate a mammalian opsin promoter because Kido et al. teach a viral vector comprising an opsin promoter is capable of selectively directing expression of therapeutic genes to photoreceptor cells (see page 841, last paragraph). One of skill in the art would want to make a vector comprising an opsin promoter to specifically express ribozymes targeted

to VEGF in retinal cells for the purpose of decreasing expression of VEGF, which contributes to disease of the eye, such as retinopathy.

Finally, one would have had a reasonable expectation of success given that Pavco et al. teach specific embodiments of ribozyme targeted to genes encoding VEGF, a gene responsible for VEGF and given that Kido et al. teach an opsin promoter incorporated into a vector directs expression of a gene in retinal cells, specifically photoreceptors and Mueller cells.

Additionally, it would have been obvious to one of skill in the art and one would have been motivated to package the ribozyme in a kit because Pavco et al. specifically teach said ribozyme targeted to VEGF would be useful as a diagnostic reagent and teach specific embodiments of treatment with a ribozyme delivered on a filtered disk to the cornea of a rat and therefore would have had a reasonable expectation of success.

Thus, in absence of evidence to the contrary, the invention would have been *prima facie* evident to one of ordinary skill in the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached at 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Kimberly Chong
Examiner
Art Unit 1635

SEAN McGARRY
PRIMARY EXAMINER
1635